REMARKS

Claims 41-42 and 67-73 are pending after entry of the foregoing amendments. The claims have been amended to indicate that the method directly measures NR2 peptides in an emergency room setting within 3 hours of stroke onset, and that the measurements are used to distinguish between ischemic and hemorrhagic stroke. Nothing in the prior art cited in the Office Action would have motivated a skilled worker to perform this diagnosis so close to the stroke because none of this prior art teaches that NR2 peptides from the brain would enter the bloodstream and be detectable within merely three hours after stroke onset. Support for the amendments is found on pages 19 and 20 of the specification.

This application stands rejected based upon Dambinova (1997), and its disclosure of testing for NR2 autoantibodies in patients who have previously suffered a stroke. The Office Action contends that this disclosure renders the claimed invention obvious because it would have motivated a skilled worker to diagnose patients using an NR2 autoantibody test. As limited, however, the claims do not cover the detection of autoantibodies and the Office Action fails to cite any motivation to detect the NR2 peptides directly. In addition, Dambinova (1997) reported the results of tests on blood samples taken weeks after the patients had suffered strokes. The Office Action fails to appreciate the difference between observing a phenomenon in patients who have previously suffered a stroke, and the use of NR2 markers in clinical practice. Absent some clinical benefit from measuring NR2 markers days or weeks after the stroke has occurred (as reported by Dambinova (1997)), there is absolutely no motivation for a diagnostics company to develop such a test, or for a skilled worker actually to perform such a diagnosis, especially within the three hour window claimed in the present application. The Office Action does not cite any motivation to apply the teachings of Dambinova (1997) to a clinically meaningful diagnostic test, or give any expectation that the teachings of Dambinova (1997) could successfully be adapted to a clinically meaningful diagnostic test. Thus, it is respectfully submitted that Dambinova (1997) fails to set forth a prima facie case of obviousness.

The present invention is based upon the inventors' discovery that NR2 markers are elevated in the blood almost immediately after a stroke occurs, and that this elevation can be used to determine whether a patient has suffered an ischemic or hemmhoragic stroke. Nothing in Dambinova (1997) or any other references cited by the Patent Office indicate that levels of these

markers would be sufficiently elevated a mere three hours after stroke onset, in time to allow a clinician to make this critical determination and administer therapy based upon whether the patient is suffering from an ischemic or hemmorhagic stroke. Indeed, it is surprising that these peptides would be able to cross the blood-brain barrier in such a short time to be clinically meaningful. Because Dambinova (1997) does not report that NR2 levels are elevated immediately following a stroke, it would not have motivated a skilled worker to perform such a test in an emergency room setting immediately after a stroke, as presently claimed.

In addition, Applicants have presented significant unexpected results associated with the use of latex agglutination that the Office Action improperly discounts. As stated in Example 6 of the specification,

> With respect to predictive efficiency, however, LA showed a surprising improvement over HPLC. For example, the LA method improved the positive predictive efficiency of patients with TIA and acute stroke on the basis of glutamate content to more than 63 % (Tables 1, 3). The negative predictive value for healthy patients was similarly improved when using the LA technique (Tables 3, 4).

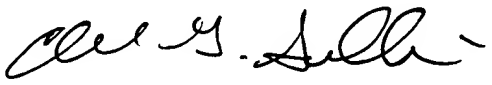
Tables 1 and 3 illustrate improved predictive value using latex agglutination for TIA patients (55.6 v. 66.4% predictive value), pre-stroke patients (44.4 v. 55.6% predictive value) and acute stroke patients (58.1 v. 64.5% predictive value). Tables 1 and 3 demonstrate that the latex agglutination method of the present invention is surprisingly superior over the HPLC methods of the prior art, and further prove the patentability of the claimed invention.

The Office Action discounts this proof based upon the disclosure in Senju (1986) of a latex agglutination test for serum C-reactive protein. However, there is no indication in Senju (1986) that NR2 testing would also benefit from the use of latex agglutination. The protein measured by Senju (1986) is vastly different in size, conformation and structure than the peptides tested using the latex agglutination process of the present invention, and does not prove one way or the other that one would have expected an increase in sensitivity from using latex agglutination with NR2 peptides. One could likely pull from the literature many other instances where the sensitivity of the test was not increased in the latex agglutination format. Applicant's improved sensitivity is surprising, and rebuts any prima facie case of obviousness that the Office Action might state. Accordingly, a prompt notice of allowance is earnestly solicited.

CONCLUSION

Applicant trusts that this communication is fully responsive to the pending Office Action. Should the Examiner have any further questions concerning this matter, the Examiner is invited to contact the undersigned at 404-572-3513. Please grant any additional extension of time required to enter this response and charge any additional fees, or credit any overpayment to Deposit Account No. 11-0980.

Respectfully submitted,



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